Group IV: Claims 19 and 29, drawn to a humanized antibody specific for HBV surface antigen pre-S1, comprising a humanized light chain variable region of SEQ ID NO: 23;

Group V: Claims 20, 21, 24-26, drawn to a gene encoding a humanized heavy chain comprising an amino acid sequence of SEQ ID NO: 20;

Group VI: Claims 20, 22, 24-26, drawn to a gene encoding a humanized heavy chain comprising an amino acid sequence of SEQ ID NO: 21;

Group VII: Claims 20, 24-26, drawn to a gene encoding a humanized heavy chain comprising an amino acid sequence of SEQ ID NO: 21 with at least one amino acid substitution;

Group VIII: Claims 23, 27, 28, drawn to a gene encoding a humanized light chain containing an amino acid sequence of SEQ ID NO: 23;

Group IX: Claim 30, drawn to a method of prevention or treatment of HBV.

Within Groups III and VII, the Examiner further required an election of one of the allegedly distinct species (a) through (i), corresponding to the various amino acid substitutions encompassed by claims 18 and 20, and listed at page 3 of the Office Action.

Applicants elect Group II, namely claims 17 and 29, with traverse.

35 U.S.C. §121 provides that "If two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." M.P.E.P. §802.01 deviates from the plain meaning of "independent and distinct" by interpreting "and" to mean "or". The Patent Office relies on the absence from the legislative history of anything contrary to this interpretation as support for their position that "and" means "or". Applicants respectfully note that this position is contrary to the rules of statutory construction. Restriction between two dependent inventions is not permissible under the plain meaning of 35 U.S.C. §121.

The Examiner alleges that the inventions of the claim groups listed above do not relate to a single inventive concept under PCT Rule 13.2, because they lack the same or corresponding special

technical features. More specifically, the Examiner alleges that the common technical feature among these inventions is the humanized antibody specific for HBV surface antigen, and that antibody is disclosed in Choi et al. (Hybridoma 17:535-570) and Ryu et al. (Human Antibodies Hybridomas 7:118-122). The Examiner therefore asserts that the groups share no common special technical feature over the prior art.

Applicants assert that restriction is improper because the subject matter of each of the claim groups is linked by the common inventive concept relating to a humanized antibody specific for surface antigen of pre-S1 of HBV. It appears the Examiner has mistaken HBV surface antigen with HBV surface antigen pre-S1.

HBV surface antigen consists of S, pre-S1 and pre-S2, and these induce antibody to neutralize and decapitate HBV. Particularly, an antibody induced by pre S region is associated with the elimination of HBV viruses and recovery from HBV infections, overcoming nonresponsiveness to S antigen (Iwarson et al., J. Med. Virol., 16:89-96, 1985). Unlike pre-S2 or S antigen, pre-S1 is exclusively present in infectious virus particles and involved in infection of human heparocytes. Therefore, it has been reported that monoclonal antibody specific for pre-S1 antigen may efficiently neuralize HBV, and the monoclonal antibody is considered to be useful in the prevention of HBV infection and the treatment of chronic hepatitis B (see Applicant's specification at page 2).

The Choi et al. reference cited by the Examiner ("Choi") does not disclose the humanized antibody specific for pre-S1 of HBV, but a human Fab monoclonal antibody specific for pre-S1 prepared by a repertoire cloning method. Moreover, Choi was published in December 1998, after the priority date of the present invention (November 19, 1998). Thus Choi is inappropriate for denying unity of the Groups of the present invention.

In addition, Ryu et al. cited by the Examiner ("Ryu") teach a humanized antibody specific for surface antigen S not for pre-S1. As described above, the S antigen is different from pre-S1 and the function thereof is far different from that of pre-S1. Thus, Ryu is also inappropriate for denying unity of the Groups of the present invention.

The humanized antibody specific for pre-S1 antigen of HBV as the common specific technical feature is distinct from the human Fab monoclonal antibody of Choi and the humanized antibody specific for S antigen of HBV of Ryu. Thus, the Examiner's assertion lacks basis.

According to M.P.E.P. §803, there are two criteria for a proper restriction requirement. First, the two inventions must be independent and distinct. In addition, there must be a serious burden on the Examiner if restriction is not required. Even if the first criterion has been met in the present case, which it has not, the second criterion has not been met.

Consequently, Applicants respectfully request the Examiner reconsider and withdraw the restriction requirement. It is also submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

GATES & COOPER LLP
Attorneys for Applicant(s)

Howard Hughes Center
6701 Center Drive West, Suite 1050
Los Angeles, California 90045
(310) 641-8797

Date: July 27, 2005

By: _____
Name: Karen S. Canady
Reg. No.: 39,927

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